Connecting via Winsock to STN

Welcome to STN International! Enter x:x

LOGINID:SSPTAJDA1614

PASSWORD:
TERMINAL (ENTER 1, 2, 3, OR ?):2

* * * * * * * * * * Welcome to STN International * * * * * * * * * *

NEWS 1		Web Page for STN Seminar Schedule - N. America
NEWS 2	APR 02	CAS Registry Number Crossover Limits Increased to 500,000 in Key STN Databases
NEWS 3	APR 02	PATDPAFULL: Application and priority number formats enhanced
NEWS 4	APR 02	DWPI: New display format ALLSTR available
NEWS 5	APR 02	New Thesaurus Added to Derwent Databases for Smooth Sailing through U.S. Patent Codes
NEWS 6	APR 02	EMBASE Adds Unique Records from MEDLINE, Expanding Coverage back to 1948
NEWS 7	APR 07	CA/CAplus CLASS Display Streamlined with Removal of Pre-IPC 8 Data Fields
NEWS 8	APR 07	50,000 World Traditional Medicine (WTM) Patents Now Available in CAplus
NEWS 9	APR 07	MEDLINE Coverage Is Extended Back to 1947
NEWS 10	JUN 16	WPI First View (File WPIFV) will no longer be available after July 30, 2010
NEWS 11	JUN 18	DWPI: New coverage - French Granted Patents
NEWS 12	JUN 18	CAS and FIZ Karlsruhe announce plans for a new STN platform
NEWS 13	JUN 18	IPC codes have been added to the INSPEC backfile (1969-2009)
NEWS 14	JUN 21	Removal of Pre-IPC 8 data fields streamline displays in CA/CAplus, CASREACT,and MARPAT
NEWS 15	JUN 21	Access an additional 1.8 million records exclusively enhanced with 1.9 million CAS Registry Numbers -- EMBASE Classic on STN
NEWS 16	JUN 28	Introducing "CAS Chemistry Research Report": 40 Years of Biofuel Research Reveal China Now Atop U.S. in Patenting and Commercialization of Bioethanol
NEWS 17	JUN 29	Enhanced Batch Search Options in DGENE, USGENE, and PCTGEN
NEWS 18	JUL 19	Enhancement of citation information in INPADOC databases provides new, more efficient competitor analyses

NEWS EXPRESS FEBRUARY 15 10 CURRENT WINDOWS VERSION IS V8.4.2,
AND CURRENT DISCOVER FILE IS DATED 15 JANUARY 2010.

NEWS HOURS STN Operating Hours Plus Help Desk Availability
NEWS LOGIN Welcome Banner and News Items

Enter NEWS followed by the item number or name to see news on that specific topic.

All use of STN is subject to the provisions of the STN customer

agreement. This agreement limits use to scientific research. Use for software development or design, implementation of commercial gateways, or use of CAS and STN data in the building of commercial products is prohibited and may result in loss of user privileges and other penalties.

* * * * * * * * * * * * * * * * STN Columbus * * * * * * * * * * * * * * * *

FILE 'HOME' ENTERED AT 12:19:59 ON 21 JUL 2010

=> file registry

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.22	0.22

FILE 'REGISTRY' ENTERED AT 12:20:11 ON 21 JUL 2010
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 19 JUL 2010 HIGHEST RN 1233120-12-1
DICTIONARY FILE UPDATES: 19 JUL 2010 HIGHEST RN 1233120-12-1

New CAS Information Use Policies, enter HELP USAGETERMS for details.

TSCA INFORMATION NOW CURRENT THROUGH January 8, 2010.

Please note that search-term pricing does apply when conducting SmartSELECT searches.

REGISTRY includes numerically searchable data for experimental and predicted properties as well as tags indicating availability of experimental property data in the original document. For information on property searching in REGISTRY, refer to:

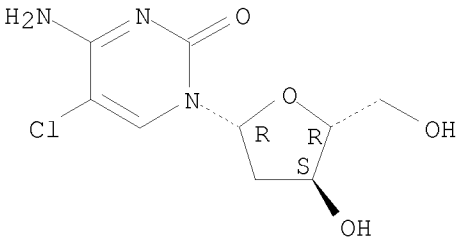
http://www.cas.org/support/stngen/stndoc/properties.html

=> s 32387-56-7/rn
L1 1 32387-56-7/RN

=> d l1

L1 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2010 ACS on STN
RN 32387-56-7 REGISTRY
ED Entered STN: 16 Nov 1984
CN Cytidine, 5-chloro-2'-deoxy- (CA INDEX NAME)
OTHER NAMES:
CN 5-Chloro-2'-deoxycytidine
CN 5-Chlorodeoxycytidine
CN NSC 371331
FS STEREOSEARCH
MF C9 H12 Cl N3 O4
LC STN Files: BEILSTEIN*, BIOSIS, BIOTECHNO, CA, CAPLUS, CASREACT, CHEMCATS, CSCHEM, DDFU, DRUGU, EMBASE, IMSDRUGNEWS, IMSRESEARCH, MEDLINE, PROUSDDR, TOXCENTER, USPATFULL
(*File contains numerically searchable property data)

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

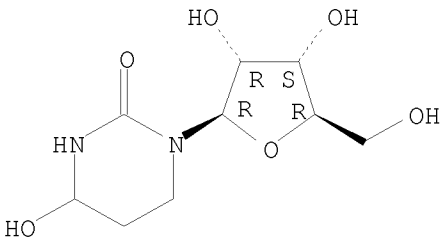
42 REFERENCES IN FILE CA (1907 TO DATE)
42 REFERENCES IN FILE CAPLUS (1907 TO DATE)

=> s tetrahydrouridine/cn
L2 1 TETRAHYDROURIDINE/CN

=> d l2

L2 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2010 ACS on STN
RN 18771-50-1 REGISTRY
ED Entered STN: 16 Nov 1984
CN Uridine, 3,4,5,6-tetrahydro- (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN 2(1H)-Pyrimidinone, tetrahydro-4-hydroxy-1-β-D-ribofuranosyl- (8CI)
OTHER NAMES:
CN 1-(β-D-Ribofuranosyl)-4-hydroxytetrahydro-1(1H)-pyrimidinone
CN 3,4,5,6-Tetrahydrouridine
CN NSC 112907
CN Tetrahydrouridine
FS STEREOSEARCH
DR 68060-67-3
MF C9 H16 N2 O6
CI COM
LC STN Files: ANABSTR, BEILSTEIN*, BIOSIS, BIOTECHNO, CA, CAPLUS, CHEMCATS, DDFU, DRUGU, EMBASE, IFICDB, IFIPAT, IFIUDB, IPA, MEDLINE, PROMT, RTECS*, SYNTHLINE, TOXCENTER, USPATFULL, USPATOLD
(*File contains numerically searchable property data)

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

113 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
113 REFERENCES IN FILE CAPLUS (1907 TO DATE)

```
=> file caplus
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                         ENTRY    SESSION
FULL ESTIMATED COST                                      10.19      10.41

FILE 'CAPLUS' ENTERED AT 12:20:40 ON 21 JUL 2010
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2010 AMERICAN CHEMICAL SOCIETY (ACS)


Copyright of the articles to which records in this database refer is
held by the publishers listed in the PUBLISHER (PB) field (available
for records published or updated in Chemical Abstracts after December
26, 1996), unless otherwise indicated in the original publications.
The CA Lexicon is the copyrighted intellectual property of the
American Chemical Society and is provided to assist you in searching
databases on STN.  Any dissemination, distribution, copying, or storing
of this information, without the prior written consent of CAS, is
strictly prohibited.

FILE COVERS 1907 - 21 Jul 2010  VOL 153 ISS 4
FILE LAST UPDATED: 20 Jul 2010  (20100720/ED)
REVISED CLASS FIELDS (/NCL) LAST RELOADED:  Apr 2010
USPTO MANUAL OF CLASSIFICATIONS THESAURUS ISSUE DATE:  Apr 2010

CAplus now includes complete International Patent Classification (IPC)
reclassification data for the second quarter of 2010.

CAS Information Use Policies apply and are available at:

http://www.cas.org/legal/infopolicy.html

This file contains CAS Registry Numbers for easy and accurate
substance identification.

=> s l1 and l2
            42 L1
           113 L2
L3          10 L1 AND L2

=> dup rem l3
PROCESSING COMPLETED FOR L3
L4           10 DUP REM L3 (0 DUPLICATES REMOVED)

=> d l4 1-10 ibib abs

L4   ANSWER 1 OF 10  CAPLUS  COPYRIGHT 2010 ACS on STN
ACCESSION NUMBER:        2008:857776  CAPLUS
DOCUMENT NUMBER:         149:167941
TITLE:                   Designer therapy of pancreatic tumors
INVENTOR(S):             Greer, Sheldon B.
PATENT ASSIGNEE(S):      University of Miami, USA
SOURCE:                  PCT Int. Appl., 56pp.
                         CODEN: PIXXD2
DOCUMENT TYPE:           Patent
LANGUAGE:                English
FAMILY ACC. NUM. COUNT:  2
PATENT INFORMATION:

     PATENT NO.          KIND   DATE        APPLICATION NO.        DATE
     ---------------     ----   --------    --------------------   --------
```

WO 2008085611 A2 20080717 WO 2007-US85613 20071127
WO 2008085611 A3 20090430
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AP, EA, EP, OA
US 20090325897 A1 20091231 US 2009-472910 20090527
PRIORITY APPLN. INFO.: US 2006-861088P P 20061127
WO 2007-US85613 A2 20071127
ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
AB Chemotherapeutic and Radiation sensitizing agents which target tumor cells, specifically, based on the elevation of enzyme pathways, provide highly selective drug therapy. These agents are combined with modulating doses of cytidine deaminase inhibitors to increase selectivity. Furthermore, high doses of these cytidine deaminase inhibitors have the potential of counteracting the aggressive and metastatic characteristics of pancreatic tumors. For tumors with high levels of cytidine deaminase, such as pancreatic tumors, this elevation provides a therapeutic approach with prodrugs that require deamination for their activation. For tumors with high levels of uridine/cytidine kinase, a different class of pyrimidine analogs can be activated selectively in tumors for a therapeutic advantage.
OS.CITING REF COUNT: 2 THERE ARE 2 CAPLUS RECORDS THAT CITE THIS RECORD (2 CITINGS)

L4 ANSWER 2 OF 10 CAPLUS COPYRIGHT 2010 ACS on STN
ACCESSION NUMBER: 2002:839583 CAPLUS
DOCUMENT NUMBER: 138:395333
TITLE: Analytical and pharmacokinetic studies with 5-chloro-2'-deoxycytidine
AUTHOR(S): Hale, JodiAnne T.; Bigelow, James C.; Mathews, Linda A.; McCormack, John J.
CORPORATE SOURCE: Department of Pharmacology and Vermont Cancer Center, University of Vermont, Burlington, VT, 05405, USA
SOURCE: Biochemical Pharmacology (2002), 64(10), 1493-1502
CODEN: BCPCA6; ISSN: 0006-2952
PUBLISHER: Elsevier Science Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB 5-Chloro-2'-deoxycytidine (NSC 371331, CDC) is in development as a possible radiosensitizing agent for cancer treatment. This paper describes preclin. studies to determine the pharmacokinetic properties of CDC and the disposition of the drug, both alone and in the presence of the metabolic modulator tetrahydrouridine (THU), a cytidine deaminase inhibitor. Detection of the drug in biol. fluids was performed by HPLC on a C-18 column, gradient elution with solvents composed of aqueous F3CCO2H and MeCN, and UV absorbance at 290 nm. Samples were processed by treatment with (NH4)2SO4 prior to injection into the HPLC system. CDC was stable in aqueous solution and in mouse plasma. High doses of CDC (100 mg/kg) were given i.v. or i.p. to mice for the determination of plasma CDC half-life (10 min). CDC was not detectable in plasma after oral administration. It was converted rapidly to 5-chloro-2'-deoxyuridine (CDU) by cytidine deaminase, and CDU was readily discernable in plasma and urine collected after i.v. and i.p.

administration of CDC. When CDC in doses ranging 5-100 mg/kg was given with 100 mg THU/kg, increased plasma levels of CDC were seen. CDC was eliminated through the kidneys, as well as by enzymic deamination, and did not bind to plasma proteins. The initial steps of the CDC metabolic pathway were determined in vitro with isolated enzymes. Cytidine deaminase from mouse kidney converted CDC to CDU; thymidine phosphorylase converted CDU to 5-chlorouracil. The conclusions of these studies are: CDC is a drug with a short half-life, and it is excreted through the kidneys, mainly in metabolite form. Administration of THU substantially increased the concns. of CDC in mouse plasma, supporting proposals that the combination of THU with CDC should be evaluated in clin. trials.

OS.CITING REF COUNT: 12 THERE ARE 12 CAPLUS RECORDS THAT CITE THIS RECORD (12 CITINGS)

REFERENCE COUNT: 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 3 OF 10 CAPLUS COPYRIGHT 2010 ACS on STN

ACCESSION NUMBER: 2001:738057 CAPLUS

DOCUMENT NUMBER: 137:17179

TITLE: 5-chlorodeoxycytidine, a tumor-selective enzyme-driven radiosensitizer, effectively controls five advanced human tumors in nude mice

AUTHOR(S): Greer, S.; Alvarez, M.; Mas, M.; Wozniak, C.; Arnold, D.; Knapinska, A.; Norris, C.; Burk, R.; Aller, A.; Dauphinee, M.

CORPORATE SOURCE: Departments of Microbiology and Immunology, Biochemistry and Molecular Biology, Radiation Oncology, Sylvester Cancer Center, University of Miami School of Medicine, Miami, FL, USA

SOURCE: International Journal of Radiation Oncology, Biology, Physics (2001), 51(3), 791-806
CODEN: IOBPD3; ISSN: 0360-3016

PUBLISHER: Elsevier Science Inc.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Purpose: The study goals were as follows: (1) to extend our past findings with rodent tumors to human tumors in nude mice, (2) to determine if the drug protocol could be simplified so that only CldC and one modulator, tetrahydrouridine (H4U), would be sufficient to obtain efficacy, (3) to determine the levels of deoxycytidine kinase and dCMP deaminase in human tumors, compared to adjacent normal tissue, and (4) to determine the effect of CldC on normal tissue radiation damage to the cervical spinal cord of nude mice. Methods and Materials: The five human tumors used were as follows: prostate tumors, PC-3 and H-1579; glioblastoma, SF-295; breast tumor, GI-101; and lung tumor, H-165. The duration of treatment was 3-5 wk, with drugs administered on Days 1-4 and radiation on Days 3-5 of each week. The biomodulators of CldC were N-(Phosphonacetyl)-L-aspartate (PALA), an inhibitor of aspartyl transcarbamoylase, 5-fluorodeoxycytidine (FdC), resulting in tumor-directed inhibition of thymidylate synthetase, and H4U, an inhibitor of cytidine deaminase. The total dose of focused irradiation of the tumors was usually 45 Gy in 12 fractions. Results: Marked radiosensitization was obtained with CldC and the three modulators. The average days in tumor regrowth delay for X-ray compared to drugs plus X-ray, resp., were: PC-3 prostate, 42-97; H-1579 prostate, 29-115; glioblastoma, 5-51; breast, 50-80; lung, 32-123. Comparative studies with PC-3 and H-1579 using CldC coadministered with H4U, showed that both PALA and FdC are dispensable, and the protocol can be simplified with equal and possibly heightened efficacy. For example, PC-3 with X-ray and (1) no drugs, (2) CldC plus the three modulators, (3) a high dose of CldC, and (4) escalating doses of CldC resulted in 0/10, 3/9, 5/10, and 6/9 cures, resp. The tumor regrowth delay data followed a similar pattern. After treating mice only 1 wk with CldC +H4U, 92% of the PC-3 tumor cells were

found to possess CldU in their DNA. The great majority of head-and-neck tumors from patient material had markedly higher levels of dC kinase and dCMP deaminase than found in adjacent normal tissue. Physiol. and histol. studies showed that CldC +H4U combined with X-ray, focused on the cervical spinal cord, did not result in damage to that tissue. Conclusions: 5-CldC coadministered with only H4U is an effective radiosensitizer of human tumors. Ninety-two percent of PC-3 tumor cells have been shown to take up ClUra derived from CldC in their DNA after only 1 wk and 2 wk of bolus i.p. injections. Enzymic alterations that make tumors successful have been exploited for a therapeutic advantage. The great electronegativity, coupled with the relatively small Van der Waal radius of the Cl atom, may result in CldC possessing the dual advantageous properties of FdC on one hand and BrdU and IdU on the other hand. These advantages include autoenhancing the incorporation of CldUTP into DNA by not only overrunning but also inhibiting the formation of competing TTP pools in tumors. A clin. trial is about to begin, with head-and-neck tumors as a first target of CldC radiosensitization.

OS.CITING REF COUNT: 4 THERE ARE 4 CAPLUS RECORDS THAT CITE THIS RECORD (4 CITINGS)

REFERENCE COUNT: 54 THERE ARE 54 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 4 OF 10 CAPLUS COPYRIGHT 2010 ACS on STN

ACCESSION NUMBER: 2000:628023 CAPLUS

DOCUMENT NUMBER: 133:219596

TITLE: Dramatic simplification of a method to treat neoplastic disease by radiation

INVENTOR(S): Greer, Sheldon B.

PATENT ASSIGNEE(S): Halogenetics, Inc., USA

SOURCE: PCT Int. Appl., 54 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000051639	A2	20000908	WO 2000-US2530	20000301
WO 2000051639	A3	20010111		
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 6933287	B1	20050823	US 2000-514278	20000228
EP 1156827	A2	20011128	EP 2000-911684	20000301
EP 1156827	B1	20060920		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, CY				
AT 339960	T	20061015	AT 2000-911684	20000301
ES 2273672	T3	20070516	ES 2000-911684	20000301
US 20040192639	A1	20040930	US 2004-779746	20040218

PRIORITY APPLN. INFO.:	US 1999-122479P	P	19990301
	US 2000-514278	A3	20000228
	WO 2000-US2530	W	20000301

AB The present invention is related to agents useful in the treatment of tumors by radiation by sensitizing tumor cells toward the radiation. The agents of the invention can perform selective tumor radiosensitization and

be involved in tumor directed hypomethylation. The agents of the invention include (a) 5-chloro-2'-deoxycytidine (CldC) administered without a cytidine deaminase inhibitor, (b) CldC administered with a cytidine deaminase inhibitor, (c) CldC and 4-N-methylamino 5-fluoro-2'-deoxycytidine (4-N-methylamino FdC), or (d) CldC and 4-N-methylamino FdC coadministered with a cytidine deaminase inhibitor. The cytidine deaminase inhibitor can be tetrahydrouridine or Zebularine. Within the scope of the invention are methods of treating tumors by administering the agents of the present invention without the need of other modulators of metabolism Another aspect of the invention is a method of hypomethylating a gene silenced in a tumor of a subject by administering the agents of the invention to the subject to reduce the aggressiveness of the tumor, the metastatic propensity of the tumor, the genetic instability of the tumor, and/or the resistance of the tumor to drug or radiation treatment. An addnl. aspect of the invention is a method of protecting normal tissues during a radiation treatment of a tumor in a subject by administering the agents of the invention to the subject before or during the radiation treatment. The agents of the invention can be combined with new sources or new schedules of radiation, and new categories of tumors can also be treated with the agents of the invention.

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 5 OF 10 CAPLUS COPYRIGHT 2010 ACS on STN

ACCESSION NUMBER: 1995:732651 CAPLUS

DOCUMENT NUMBER: 123:187874

ORIGINAL REFERENCE NO.: 123:33089a,33092a

TITLE: Five-chlorodeoxycytidine and biomodulators of its metabolism result in fifty to eighty percent cures of advanced EMT-6 tumors when used with fractionated radiation

AUTHOR(S): Greer, Sheldon; Schwade, James; Marion, H. Stan

CORPORATE SOURCE: Dep. Microbiol. Immunol., Univ. Miami Sch. Med., Miami, FL, USA

SOURCE: International Journal of Radiation Oncology, Biology, Physics (1995), 32(4), 1059-69
CODEN: IOBPD3; ISSN: 0360-3016

PUBLISHER: Pergamon

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Purpose: to extend our findings in previous radiation and biochem. studies with five rodent tumors, in which we used one and occasionally two or three irradns. The extent of control of the EMT-6 mammary adenocarcinoma was determined using fractionated radiation (12 irradns.) over a 3-wk period using the radiosensitizer 5-chloro-2'-deoxycytidine (CldC) and biomodulators of its metabolism: N-(phosphonacetyl)-L-aspartate (PALA), tetrahydrouridine and 5-fluoro-2'-deoxycytidine (FdC). Methods and Materials: mammary adenocarcinoma EMT-6 tumors implanted 1 wk prior to therapy in BALB/c mice were subjected to single daily doses of focused radiation, not exceeding a total of 60 Gy, on days 2-5 of each wk. PALA was administered on the first day of therapy. 5-Fluoro-2'-deoxycytidine and CldC were administered in the morning and afternoon, resp., of the next 2 days, and CldC was administered on the fourth day. Tetrahydrouridine was always coadministered with FdC or CldC. Drug and radiation treatments overlapped for 3 wks. Results: fifty to 80% cures (usually 70%) were obtained with no apparent morbidity and the same moderate weight loss that occurs with radiation alone. Neither tumor regrowth delay nor cures were obtained with drugs or radiation alone. An apparent threefold dose increase effect was obtained with the end point: "days to reach 4 times initial tumor volume". Increasing the radiation dose threefold (without drugs) resulted in four out of five deaths; increasing the dose twofold (without drugs) resulted in extensive weight loss and hair

loss in the entire ventral area and no cures. Increasing the dose of drugs or radiation 1.5-fold, in the complete protocol, did not result in increased morbidity. Comparative studies with Iododeoxyuridine demonstrate the heightened efficacy of CldC. Conclusions: one cannot achieve the same results obtained with CldC and the modulators by merely increasing the dose of radiation. There is a significant window of safety in this approach. The evidence we have obtained with EMT-6, the fifth rodent tumor we have studied with CldC, as well as the demonstrated and proposed reasons for its superior efficacy over 5-Iododeoxyuridine (and 5-Bromodeoxyuridine), drugs in current use, indicate that CldC will allow more aggressive treatment of human tumors with radiation than is now feasible.

OS.CITING REF COUNT: 9 THERE ARE 9 CAPLUS RECORDS THAT CITE THIS RECORD (9 CITINGS)

L4 ANSWER 6 OF 10 CAPLUS COPYRIGHT 2010 ACS on STN
ACCESSION NUMBER: 1989:435901 CAPLUS
DOCUMENT NUMBER: 111:35901
ORIGINAL REFERENCE NO.: 111:6085a,6088a
TITLE: Selective radiosensitization and cytotoxicity of human melanoma cells using halogenated deoxycytidines and tetrahydrouridine
AUTHOR(S): Lawrence, Theodore S.; Davis, Mary A.
CORPORATE SOURCE: Dep. Radiat. Oncol., Univ. Michigan, Ann Arbor, MI, 48109, USA
SOURCE: International Journal of Radiation Oncology, Biology, Physics (1989), 16(5), 1243-6
CODEN: IOBPD3; ISSN: 0360-3016
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The halogenated pyrimidines 5-chloro-2'-deoxycytidine (CldCyd) and 5-bromo-2'-deoxycytidine (BrdCyd) can act as radiosensitizers and cytotoxic agents. It was hypothesized that tumor cells and normal cells might use different metabolic pathways to incorporate these halogenated deoxycytidines into DNA. This difference could potentially be exploited to produce selective radiosensitization and cytotoxicity of human tumor cells compared to normal human fibroblasts. This hypothesis was tested using 2 human melanoma cell lines and 2 normal fibroblast cell lines. CldCyd or BrdCyd alone caused both cytotoxicity and radiosensitization of tumor and normal cells. The addition of the cytidine deaminase inhibitor tetrahydrouridine (H4U) significantly protected the normal cells but had relatively little effect on the tumor cells. These data indicate that it may be possible to exploit differences between the pyrimidine metabolism of normal cells and melanoma cells to improve the therapeutic index of halogenated pyrimidines both as radiosensitizers and as cytotoxic agents.
OS.CITING REF COUNT: 3 THERE ARE 3 CAPLUS RECORDS THAT CITE THIS RECORD (3 CITINGS)

L4 ANSWER 7 OF 10 CAPLUS COPYRIGHT 2010 ACS on STN
ACCESSION NUMBER: 1986:438294 CAPLUS
DOCUMENT NUMBER: 105:38294
ORIGINAL REFERENCE NO.: 105:6285a,6288a
TITLE: In vitro and in vivo radiation sensitization by the halogenated pyrimidine 5-chloro-2'-deoxycytidine
AUTHOR(S): Russell, Kenneth J.; Rice, Glenn C.; Brown, J. Martin
CORPORATE SOURCE: Med. Cent., Stanford Univ., Stanford, CA, 94305, USA
SOURCE: Cancer Research (1986), 46(6), 2883-7
CODEN: CNREA8; ISSN: 0008-5472
DOCUMENT TYPE: Journal
LANGUAGE: English
AB 5-Chloro-2'-deoxycytidine (Cld/Cyd) is hypothesized to have preferential incorporation into tumor DNA on the basis of elevated

deoxycytidine-5'-phosphate deaminase and deoxycytidine kinase levels in tumors. Radiosensitization by Cld/Cyd was evaluated in exponentially growing Chinese hamster ovary cells by determining the ratio of radiation doses in control and treated cells to produce the same degree of cell killing (sensitizer enhancement ratio). Sensitizer enhancement ratios of 1.2-1.8 are seen at Cld/Cyd concns. of 3-100 μM, 64 h incubation, and 200-600 cGy x-irradiation Coincubation with tetrahydrouridine (H4Urd), a proposed inhibitor of Cld/Cyd catabolism by plasma cytidine deaminase, resulted in no enhanced drug or radiation cytotoxicity. C3H mice given implants of RIF-1 tumors received 72-h continuous i.p. infusions of Cld/Cyd with or without H4Urd, or 5-bromo-2'-deoxyuridine (BrdUrd). Excised tumors were irradiated as single cell suspensions in vitro. Infusions of equimolar (0.4 mmol/kg/day) Cld/Cyd or BrdUrd resulted in greater radiosensitization by BrdUrd with no potentiation of Cld/Cyd by coinfusion with 0.8 mmol/kg/day H4Urd. Infusions with equitoxic doses of Cld/Cyd (0.8 mmol/kg/day) or BrdUrd (0.4 mmol/kg/day) yielded equal BrdUrd and Cld/Cyd sensitizer enhancement ratios of 1.6, without H4Urd potentiation of Cld/Cyd. Fluorescence-activated cell sorter anal. of tumor cell suspensions using a monoclonal antibody reactive with BrdUrd and Cld/Cyd disclosed a population of noncycling cells in tumors treated with Cld/Cyd/H4Urd that is not seen in tumors exposed to either BrdUrd or Cld/Cyd alone.

OS.CITING REF COUNT: 2 THERE ARE 2 CAPLUS RECORDS THAT CITE THIS RECORD (2 CITINGS)

L4 ANSWER 8 OF 10 CAPLUS COPYRIGHT 2010 ACS on STN

ACCESSION NUMBER: 1986:605494 CAPLUS
DOCUMENT NUMBER: 105:205494
ORIGINAL REFERENCE NO.: 105:33081a,33084a
TITLE: Sensitization to x ray by 5-chloro-2'-deoxycytidine co-administered with tetrahydrouridine in several mammalian cell lines and studies of 2'-chloro derivatives
AUTHOR(S): Perez, Liliana M.; Greer, Sheldon
CORPORATE SOURCE: Sch. Med., Univ. Miami, Miami, FL, 33101, USA
SOURCE: International Journal of Radiation Oncology, Biology, Physics (1986), 12(8), 1523-7
CODEN: IOBPD3; ISSN: 0360-3016
DOCUMENT TYPE: Journal
LANGUAGE: English

AB 5-Chloro-2'-deoxycytidine (CldC) + tetrahydrouridine (H4U) sensitizes mammalian cells (HEp-2, RIF-1, S-180) to x-rays. This sensitization, as demonstrated previously with HEp-2 cells, is heightened when cells are preincubated with inhibitors of pyrimidine synthesis. CHO cells, which intrinsically lack both cytidine deaminase (CD) and deoxycytidylate deaminase (dCMPD), are sensitized to x-rays by 5-chlorodeoxyuridine (CldU) but display no sensitization with CldC + H4U. The presence and level of these deaminases appears to correlate with x-ray sensitization in cell culture. From expts. in cell culture, it can be inferred that one pathway of conversion, deoxycytidine kinase → dCMPD or CD → thymidine kinase, may be sufficient for metabolizing CldC to a radiosensitizer. However, if both pathways are blocked, as in CHO cells, no x-ray sensitization results. In addition to HEp-2 cells, which are extremely elevated in both CD and dCMPD activities, the sensitization of S-180 and RIF-1 cells to x-rays by CldC + H4U was examined Both cell lines possess an enzymic profile consistent with their sensitization to x-rays by CldC + H4U. Dose enhancement ratios of 1.5-1.9 for cells treated with CldC + H4U and ratios of 2.0-2.7 for cells pre-treated with inhibitors of pyrimidine synthesis prior to CldC + H4U have been obtained. 2',5'-Dichloro-2'-deoxycytidine and 5-bromo-2'-chloro-2-deoxyuridine were x-ray sensitizers of mammalian cells. The strategy that is proposed with CldC + H4U and the related 2'-chloro derivs., based on the elevation of CD

and dCMPD in human tumors, offers a degree of selectivity that is not necessarily related to differences in cell kinetics, such that malignancies other than brain tumors may be amenable to this therapy.

OS.CITING REF COUNT: 2 THERE ARE 2 CAPLUS RECORDS THAT CITE THIS RECORD (2 CITINGS)

L4 ANSWER 9 OF 10 CAPLUS COPYRIGHT 2010 ACS on STN

ACCESSION NUMBER: 1985:476273 CAPLUS
DOCUMENT NUMBER: 103:76273
ORIGINAL REFERENCE NO.: 103:12215a,12218a
TITLE: Method and materials for sensitizing neoplastic tissue to radiation
INVENTOR(S): Greer, Sheldon B.
PATENT ASSIGNEE(S): USA
SOURCE: PCT Int. Appl., 31 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

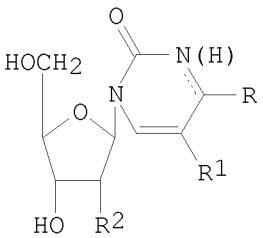
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 8501871	A1	19850509	WO 1984-US1735	19841026
W: AU, BR, DK, FI, JP, US				
RW: AT, BE, CH, DE, FR, GB, LU, NL, SE				
AU 8436107	A	19850522	AU 1984-36107	19841026
AU 583801	B2	19890511		
EP 160079	A1	19851106	EP 1984-904049	19841026
EP 160079	B1	19900131		
R: AT, BE, CH, DE, FR, GB, LI, LU, NL, SE				
JP 61500224	T	19860206	JP 1984-504070	19841026
JP 05086376	B	19931210		
AT 49894	T	19900215	AT 1984-904049	19841026
US 4894364	A	19900116	US 1985-749540	19850624
CA 1269658	A1	19900529	CA 1985-494396	19851101

PRIORITY APPLN. INFO.:

US 1983-545693	A2	19831026
EP 1984-904049	A	19841026
WO 1984-US1735	A	19841026

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

GI



I

AB I (R = NH2 or O, R1 and R2 = H or halogen) for use in pharmaceutical compns. are radiosensitizers. The concentration of the active ingredient in the composition is 0.01-25% by weight depending on the route of administration, severity of the case, frequency of administration, etc. The radiation dose, x- or γ-ray will be either the same or one-fourth to three-fourths the dose given to patients not receiving the pretreatment sensitizer, and this will result in either a more effective tumor kill or

an equal tumor kill but with less damage to underlying tissues. In a toxicity study in animals injected i.p. with N-(phosphonoacetyl)-L-aspartate [51321-79-0] (pretreatment agent) 200, followed 24 h later with i.p. 5-fluoro-2'-deoxyuridine (I; R = NH2, R1 = F, R2 = H) [50-91-9] 50, and 4 h later i.p. 5-chloro-2'-deoxycytidine (I; R = NH2, R1 = Cl, R2 = H) [32387-56-7] 500 coadministered with tetrahydrouridine [18771-50-1] 100 mg, the last 2 compds. administered at the same concentration twice at 10 h intervals, a 4% weight loss occurred which is trivial compared to normal weight loss which occurs from administration of antitumor agents in radiation therapy.

OS.CITING REF COUNT: 5 THERE ARE 5 CAPLUS RECORDS THAT CITE THIS RECORD (5 CITINGS)

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 10 OF 10 CAPLUS COPYRIGHT 2010 ACS on STN

ACCESSION NUMBER: 1984:625942 CAPLUS

DOCUMENT NUMBER: 101:225942

ORIGINAL REFERENCE NO.: 101:34219a,34222a

TITLE: Marked radiosensitization of cells in culture to x-ray by 5-chlorodeoxycytidine coadministered with tetrahydrouridine, and inhibitors of pyrimidine biosynthesis

AUTHOR(S): Perez, Liliana M.; Mekras, John A.; Briggle, Thomas V.; Greer, Sheldon

CORPORATE SOURCE: Sch. Med., Univ. Miami, Miami, FL, 33101, USA

SOURCE: International Journal of Radiation Oncology, Biology, Physics (1984), 10(8), 1453-8
CODEN: IOBPD3; ISSN: 0360-3016

DOCUMENT TYPE: Journal

LANGUAGE: English

AB To overcome the problem of rapid catabolism and general toxicity encountered with 5-halogenated analogs of deoxyuridine (5-bromo, chloro, or iododeoxyuridine), which has limited their use as tumor radiosensitizers, 5-chlorodeoxycytidine (CldC) with tetrahydrouridine (H4U) is utilized. In x-irradiation studies with HEp-2 cells, limited to 1 or 2 radiation doses, 3.0-3.8 apparent dose enhancement ratios (these represent upper limits) were obtained when cells are preincubated with inhibitors of pyrimidine biosynthesis, i.e., N-(phosphonacetyl)-L-aspartate (PALA) and 5-fluorodeoxyuridine (FdU) or 5-fluorodeoxycytidine (FdC) + H4U. Optimum conditions for radiosensitization are PALA (0.1 mg/mL) 18-20 h prior to FdU (0.1 μM) or FdC (0.02 μM) + H4U (0.1 mM) followed 6 h later by CldC (0.1-0.2 mM) + H4U (0.1 mM) for 56-68 h. Viabilities of 10-15% were obtained for drug-treated unirradiated cells. Enzymic studies indicate that this toxicity may be tumor selective. CldC + H4U alone (at these concns.) results in 20% substitution of CldU for thymidine in DNA (determined by HPLC anal.). Preliminary toxicity studies indicate that mice will tolerate treatment protocols involving a single dose of PALA (200 mg/kg) followed by a dose of FdU (50 mg/kg) and 3 cycles of CldC (500 mg/kg) + H4U (100 mg/kg) at 10 h intervals, with marginal weight loss (4%). In this approach, preferential conversion of CldC to CldUTP at the tumor site is obtained by taking advantage of quant. differences in enzyme levels between tumors and normal tissues.

OS.CITING REF COUNT: 4 THERE ARE 4 CAPLUS RECORDS THAT CITE THIS RECORD (4 CITINGS)

=> d his

(FILE 'HOME' ENTERED AT 12:19:59 ON 21 JUL 2010)

```
     FILE 'REGISTRY' ENTERED AT 12:20:11 ON 21 JUL 2010
L1             1 S 32387-56-7/RN
L2             1 S TETRAHYDROURIDINE/CN

     FILE 'CAPLUS' ENTERED AT 12:20:40 ON 21 JUL 2010
L3            10 S L1 AND L2
L4            10 DUP REM L3 (0 DUPLICATES REMOVED)

=>

---Logging off of STN---



=>
Executing the logoff script...


=> LOG Y

COST IN U.S. DOLLARS                            SINCE FILE      TOTAL
                                                   ENTRY    SESSION
FULL ESTIMATED COST                                36.00      46.41

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)      SINCE FILE      TOTAL
                                                   ENTRY    SESSION
CA SUBSCRIBER PRICE                                -8.50      -8.50

STN INTERNATIONAL LOGOFF AT 12:26:25 ON 21 JUL 2010
```